GEORGIA INSTITUTE OF TECHNOLOGY
OFFICE OF CONTRACT ADMINISTRATION

SPONSORED PROJECT INITIATION

Date: 4/19/77

Project Title: "Analysis of Flow Disorder in Occlusive Vascular Disease with Development of Pulsed Doppler Ultrasound to Measure Turbulent Blood Flow Noninvasively."

Project No: E-16-615

Green Cl

Project Director: Dr. D. P. Giddens and Dr. R. F. Mabon

Sponsor: National Science Foundation, Washington, D. C. 20550

Agreement Period: From 3/15/77 Until 8/31/79
(24-month budget period plus flexibility period.)

Type Agreement: Grant No. ENG76-23876

Amount: $98,600 NSF
2,488 GIT (E-16-385)
$101,088 TOTAL

Reports Required: Annual Technical Letter; Final Technical Report.

Sponsor Contact Person (s):

Technical Matters

Contractual Matters
(thru OCA)

James L. Bostick
Grants Officer
National Science Foundation
Washington, D. C. 20550

Defense Priority Rating: None

Assigned to: Aerospace Engineering (School/Laboratory)

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CA–3 (3/76)

GEORGIA INSTITUTE OF TECHNOLOGY
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SPONSORED PROJECT TERMINATION

Date: January 11, 1980

Project Title: "Analysis of Flow Disorder in Occlusive Vascular Disease with Development of Pulsed Doppler Ultrasound to Measure Turbulent Blood Flow Noninvasively."

Project No: E-16-615

Project Director: Dr. D.P. Giddens and Dr. R.F. Mabon

Sponsor: National Science Foundation, Washington, D.C. 20550

Effective Termination Date: 8/31/79

Clearance of Accounting Charges: 8/31/79

Grant/Contract Closeout Actions Remaining:

_ Final Invoice and Closing Documents
X Final Fiscal Report
_ Final Report of Inventions
_ Govt. Property Inventory & Related Certificate
_ Classified Material Certificate
_ Other ____________

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CA-4 (1/79)

NATIONAL SCIENCE FOUNDATION
Washington, D.C. 20550

FINAL PROJECT REPORT
NSF FORM 98A

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PART I–PROJECT IDENTIFICATION INFORMATION

1. Institution and Address	2. NSF Program	3. NSF Award Number
	4. Award Period From 3/15/77 To 8/31/79	5. Cumulative Award Amount $98,600

6. Project Title

Analysis of Flow Disorder in Occlusive Vascular Disease with Development of Pulsed Doppler ultrasound to Measure Turbulent Blood Flow Noninvasively

PART II–SUMMARY OF COMPLETED PROJECT *(FOR PUBLIC USE)*

Previous research has demonstrated that unusual disturbances in blood velocity are a consequence of the early development of arterial disease. If the conditions under which disturbances occur can be ascertained and if a noninvasive means for accurately measuring these can be developed, a useful method for detection of presymptomatic arterial disease may result. The objectives of this study were therefore threefold: (1) to investigate the nature and behavior of flow disturbances caused by arterial constrictions, or stenoses, in pulsatile flow; (ii) to target a specific and relevant arterial site for detailed study; and (iii) to extend the capability of pulsed Doppler ultrasound to the point of allowing accurate measurement of turbulence. These objectives were obtained by flow visualization techniques and laser Doppler anemometry in laboratory models of stenoses and the human carotid artery and by theoretical research to establish a comprehensive framework for velocity measurements with pulsed Doppler ultrasound. The research to date as yielded: descriptions of flow disturbances which other investigators are using in the development of clinical methods for early disease detection; measurement of steady flow in the carotid artery which demonstrate that the favored region of disease development is one which has separated and/or oscillating flow patterns; and a theoretical model for ultrasound measurements which has been proven highly accurate on simulated Doppler signals. These findings have important implications to the understanding and detection of arterial disease.

PART III–TECHNICAL INFORMATION *(FOR PROGRAM MANAGEMENT USES)*

1. ITEM *(Check appropriate blocks)*	NONE	ATTACHED	PREVIOUSLY FURNISHED	TO BE FURNISHED SEPARATELY TO PROGRAM Check (√)	Approx. Date
a. Abstracts of Theses		X			
b. Publication Citations		X			
c. Data on Scientific Collaborators		X			
d. Information on Inventions	X				
e. Technical Description of Project and Results				X	1/1/80
f. Other *(specify)*					

2. Principal Investigator/Project Director Name *(Typed)*	3. Principal Investigator/Project Director Signature	4. Date
Don P. Giddens		11/26/79

FINAL REPORT

NATIONAL SCIENCE FOUNDATION GRANT ENG76-23876

ANALYSIS OF FLOW DISORDER IN OCCLUSIVE VASCULAR DISEASE WITH DEVELOPMENT OF PULSED DOPPLER ULTRASOUND TO MEASURE TURBULENT BLOOD FLOW NONINVASIVELY

by

D.P. Giddens and R.F. Mabon

School of Aerospace Engineering
Georgia Institute of Technology

January 1980

INTRODUCTION

This document is a summary final report on NSF Grant ENG76-23876, "Analysis of Flow Disorder in Occlusive Vascular Disease with Development of Pulsed Doppler Ultrasound to Measure Turbulent Blood Flow Noninvasively". The research can be broadly categorized into two areas: fluid dynamic studies and improvements in pulsed Doppler ultrasound. These, in turn, are subdivided into specific objectives. This report summarizes the results of research in these areas and provides references to more detailed documentation in published papers and Ph.D. theses.

The investigators are grateful for the support provided by the National Science Foundation and sincerely hope that these results will contribute to a better understanding of the role of fluid dynamics in arterial disease.

RESULTS OF RESEARCH

A. *In Vivo* Studies of Poststenotic Flows

At the initiation of Grant ENG76-23876 hot film measurements of centerline velocity distal to stenoses imposed on the descending thoracic aortas of dogs were available on FM tape. Although considerable analysis was complete at that time, the full power of flow disturbance analysis had not been brought to bear upon that data. Therefore, initial efforts under this grant were to further study the existing *in vivo* data. The results of this study are contained in References A.2 and B.2 and may be summarized as follows:

1. Ensemble average waveforms showed the existence of coherent disturbances for mild and moderate stenoses.
2. The deceleration phase of systole was more unstable than the acceleration phase.
3. Turbulence existed in the deceleration phase for stenoses as mild as 20 percent reduction in cross-sectional area.
4. For mild stenoses (<40 percent) the acceleration phase of systole contained little flow disorder.
5. The evolution of rms disturbance velocities and energy spectra during the cycle was a sensitive indicator of the existence of stenoses.

The results demonstrate the ability of ensemble averaging techniques to identify coherent and disordered disturbances in a poststenotic flow and also serve to give encouragement that flow disturbance analysis may prove a useful tool in the identification of atherosclerotic plaques, particularly at a relatively early stage of development.

B. In Vitro Studies of Poststenotic Flows

Since conditions in the dog aorta are difficult to control, it was deemed prudent to investigate poststenotic flows in laboratory models. This was accomplished with a laser Doppler anemometer system, employing pulsatile flow of a water/glycerin mixture through a plexiglas tube. A replaceable test section which contained a smoothly contoured constriction of either 25, 50 or 75 percent reduction in cross-sectional area was employed, and centerline velocity measurements were taken at various stations downstream. Details of this study are contained in References A.2 and C.1. The results are summarized as follows.

1. Three clearly distinct flow disturbances may exist in the pulsatile, poststenotic field: a starting structure; a laminar instability; and turbulence.
2. The starting structure is coherent and reproducible with each cycle, and it persists for quite some distance for mild constrictions (25 and 50 percent).
3. The laminar instability which may exist in the region of peak velocity, preferentially occurring during the early stages of flow deceleration, is the precursor of turbulence rather than the starting structure, in the case of mild constrictions (25 and 50 percent).
4. Intense turbulence occurs under the given experimental conditions for stenoses which would likely be "hemodynamically insignificant" by current clinical standards (75 percent reduction in area). Turbulence in this case appears to be triggered by the starting structure although a laminar oscillation exists in the very near poststenotic field.
5. Ensemble averaging and Fourier transform techniques are extremely useful, if not mandatory, in determining the nature of poststenotic disturbances.

Again, the in vitro studies imply that flow disturbance identification - particularly of coherent structures - might be useful in lowering the threshold of recognition of arterial disease, provided the measurements can be achieved noninvasively. Before it becomes a useful clinical tool, however, more must be known concerning the fluid dynamics of specific arterial sites, such as the carotid artery, since flow disturbances will depend strongly on local geometry and flow conditions.

C. Hemodynamics of the Carotid Artery

In an effort to bring the fluid dynamic studies to bear upon a relevant need, the carotid arterial complex was selected for detailed study. This complex includes the common, internal and external carotid arteries and the carotid sinus. Atherosclerosis of this vascular site is frequently responsible for stroke, and the resulting morbidity and mortality are well-documented. Additionally, these vessels are near the body surface and are therefore accessible to study with ultrasound. However, the fluid dynamics of this complex branch are not yet known, and it was decided to initiate a long-range, fundamental study of carotid artery hemodynamics.

The first step undertaken was to construct a representative flow model. To this end numerous biplanar angiograms of human subjects ranging from infancy to age 70 were studied quantitatively to define an "average" geometry. These efforts are documented in Reference A.4. It is important to emphasize that the human anatomy varies tremendously, and the resulting carotid model is not assumed to be an all-encompassing representation. It does, however, possess important features and considerable effort has gone into making the geometry realistic.

The initial flow studies have just recently been completed. Investigations began with steady flow at several Reynolds numbers typical of those found in the human carotids and at flow division ratios into the internal and external branches which are representative of the physiologic state. Flow visualization was achieved with hydrogen bubbles and with dye injections, and velocity profiles were measured with the laser Doppler anemometer. Detailed results of these studies are given in References A.4 and B.8, and a summary of important findings follows:

1. Flow separation, accompanied by complex helical secondary flows, occurred in the carotid sinus under all flow conditions studied.
2. Flow separation occurred in the external carotid vessel only when very low flow rates were directed into that branch.
3. Although the sinus contained separated and reversed flows, this was not a region of recirculation, i.e. dye particles were not entrapped in the sinus.

4. Flow direction near the sinus walls varied considerably with flow division and Reynolds number. This may indicate that in a pulsatile flow wall shear stress vectors in the sinus will change direction during each flow cycle.
5. Shear stress along the walls near the apex of the bifuration was relatively high and unidirectional while low shear stresses of varying direction occur in the separated flow region of the sinus. In the internal carotid artery, distal to the sinus, the area reduction leads to relatively high, unidirectional wall shear stresses.
6. Only for the highest Reynolds number cases was any unsteadiness seen in the flow, indicating that flow may be inherently laminar in this region in the physiologic state.

These conclusions are based upon steady flow through a rigid carotid model and hence must not be extrapolated carelessly to the human case. The next phase of the study will be in pulsatile flow and later work will include experiments with models which have stenoses present. However, the results to date give new insight into carotid hemodynamics and provide a foundation for further studies.

D. Phase-Lock Loop Processing of Pulsed Doppler Ultrasound

Since fluid dynamic studies were pointing toward the possibility of employing flow disturbance analysis as a diagnostic tool, attention was focused upon methods to make accurate velocity measurements noninvasively; and Doppler ultrasound was the obvious candidate. However, at the outset of this research program existing ultrasound systems did not adequately measure turbulence. Initial studies in this area borrowed technology from laser Doppler anemometry and applied phase-lock loop (PLL) processing to pulsed Doppler ultrasound signals. The results were a substantial improvement in the ability of the ultrasonic device to accurately follow rapid velocity fluctuations. The procedure consisted of upshifting Doppler ultrasound signals to a higher frequency which would be acceptable to a DISA Mark II frequency tracker. Amplitude balancing between the shift frequency and Doppler frequency is required. Measurements of turbulence with this modified ultrasound were compared with data taken by hot film and laser Doppler anemometry for steady and pulsatile flow conditions in plexiglas tubes. Results are reported in References A.2 and B.7 and are summarized below.

1. Turbulent energy spectra calculated from pulsed Doppler/PLL velocity measurements in fully developed pipe flow agree well with laser Doppler and hot film anemometer results over a Reynolds number range from 6,000 to 15,000.

2. Turbulence intensity measurements in pipe flow with the ultrasound system agree with published data in the literature.
3. Flow field measurements distal to a 50 percent stenosis in pulsatile flow show good agreement between LDA and ultrasound determinations of turbulence velocity.
4. For intensely turbulent flows, signal dropout is a problem when applying the phase-lock loop to Doppler ultrasound signals.
5. Results are somewhat sensitive to tracker bandwidth, and best data are obtained by minimizing signal dropout. However, this sensitivity indicates that signal processing is not yet optimum, and a clear separation of signal and noise at high frequencies has not been achieved under all flow conditions.

PLL tracking of Doppler ultrasound signals thus represents substantial improvement over zero crossing detectors which are currently in use. However, there is also substantial room for improvement. It seems that further progress depends upon a better understanding of the interrelationships among flow phenomena, scattering behavior, and signal processing. This point will be discussed in the next section.

E. Digital First Moment Processing of Doppler Ultrasound

This aspect of the research program seeks to develop a comprehensive theory for the measurement of rapidly fluctuating fluid velocities, to implement the theory with digital processing, and to define limits for turbulence measurements with ultrasound. The theoretical model assumes that particles scatter ultrasound incoherently so that the normalized power spectrum of the return Doppler signal is a measure of the probability distribution of particle velocities within the sample volume. This draws a direct analogy between the molecular velocity distribution in statistical gas dynamics and the velocity distribution of ultrasound scatterers. However, several realities complicate the straightforward application of the theory: the validity of Rayleigh scattering on a short time (almost "instantaneous") basis; the nonuniformity of the sample volume; sampling constraints; and the fluid dynamics of the process being studied.

Work to date has applied the "instantaneous" first moment concept to the idealized case of a uniform acoustic field within the sample volume and has treated electronically synthesized Doppler signals in an effort to separate problems of signal processing from problems of mechanics. Details of the research are found in References A.3 and B.5. Briefly, the important results obtained at this stage of research are as follows:

1. A theoretical model for interpreting Doppler ultrasound signals from a statistical fluid mechanics viewpoint has been postulated and implemented on a digital computer.
2. A Doppler signal synthesizer has been constructed which allows separation of signal processing and mechanics problems.
3. The first moment theory has accurately calculated turbulent velocities, within design sampling constraints, from synthesized Doppler signals, thus establishing the accuracy of the signal processing methods.
4. Digital windows have been found to be useful in treating the Doppler signal.

It is emphasized that this research does not seek to provide a practical tool for frequency-to-voltage conversion per se, and the basic problem in Doppler ultrasound is not simply how fast a Doppler frequency may be measured. Rather, the fundamental difficulty is the proper interpretation of the Doppler signal from the fluid mechanics standpoint; and it is within this context that the digital first moment approach is significant. An appealing aspect is its straightforward design. For a given ultrasound transmission frequency the system accuracy, frequency resolution and frequency response are controlled by selection of the sampling parameters and choice of sampling window. Furthermore, as additional knowledge of scattering phenomena is gained, methods for spectral correction due to various contributions such as nonuniform insonation and transit time effects can be implemented in digital processing much more readily than with analog schemes. Finally, the digital first moment method is a direct computational representation of a theoretical model, and it provides a tool to assist in improvements in this model. Future studies will be directed towards the mechanics of the scattering process and how these can be incorporated into the theoretical scheme.

SIGNIFICANCE

In reviewing the research accomplishments under this grant it is the opinion of the investigators that four significant advances have been made which contribute to a better understanding of the role of fluid dynamics in arterial disease.

1. Pulsed Doppler Ultrasound/Phase-Lock Loop Measurements of Turbulence. The use of an advanced phase-lock loop frequency tracker for processing pulsed Doppler ultrasound signals has resulted in accurate measurements of turbulent velocities with ultrasound. To the knowledge of the investigators this is the first time this has been achieved, and it represents a significant improvement in noninvasive blood velocity measurement. Given the increasing proliferation of Doppler ultrasound instruments, this could have important impact upon clinical measurements in the future; and, additionally, it provides an improved tool for hemodynamic research.

2. Digital First Moment Theory of Velocity Measurement with Doppler Ultrasound. Although a first moment approach for estimating velocity from the Doppler spectrum has been postulated by several other investigators, the hypothesis has previously been that of essentially steady flow. The extension of the first moment concept to a flow in which the velocity is rapidly varying may represent an important advancement in a unified theoretical model for velocity measurement with Doppler ultrasound. Although our theoretical model has been proven on synthesized Doppler signals, it has yet to be established for actual flows. If this can be achieved, the digital first moment theory can be employed, not only to measure velocity, but to establish limits of accuracy and to provide a framework within which further improvements can be made in ultrasound systems. This theoretical model bears not only upon medical ultrasound but may be of value in a broader sense in that flow processes which are not amenable to velocity meaurement by other means might be studied with Doppler ultrasound.

3. Flow Disturbance Analysis and Its Relationship to Detection of Atherosclerosis. The existence of flow disturbances distal to mild stenoses in animal and laboratory models has been convincingly demonstrated, and analysis techniques for identifying and classifying these disturbances have been developed. Mild stenoses were shown to produce coherent disturbance structures during the starting process of each cycle and, under some conditions, turbulence during the deceleration phase of the velocity waveform. If these findings carry over to a specific site in the human vasculature, such as the carotid artery, a valuable diagnostic tool may result. The investigators view flow disturbance analysis, when coupled with advanced Doppler ultrasound measurement methods, as a potentially significant complement to imaging methods.

4. Hemodynamics of the Carotid Arteries. The results of this study have bearing on the early detection of atherosclerosis and the puzzle of atherogenesis. The steady flow results from the carotid model demonstrate complex flow patterns with zones of low, multidirectional wall shear stress in regions of the bifurcation prone toward atherosclerosis and with areas of high, unidirectional wall shear stress in the neighborhood of the apex of the bifurcation, a location usually spared from disease. Flow was found to be laminar under virtually all conditions studied except for slight instabilities in the sinus for the highest physiologically realistic Reynolds numbers. Thus, it might be anticipated that plaque development may create notable flow disturbances. Research must continue to include pulsatile flow and to search for mechanisms relating the flow environment to the pathology of the arterial wall.

PUBLICATIONS AND PRESENTATIONS

The following publications have resulted wholly or in part from research performed under this grant.

A. Ph.D. Theses

1. M.D. Deshpande; "Steady Laminar and Turbulent Flow Through Vascular Stenosis Models", 1977.

2. A.M.A. Khalifa; "The Role of Flow Disorder in the Noninvasive Detection of Atherosclerosis", 1978.

3. V. Saxena; "Turbulence Measurements using Pulsed Doppler Ultrasound", 1978.

4. K. Balasubramanian; "An Experimental Investigation of Steady Flow at an Arterial Bifurcation", 1979.

B. Papers Published

1. M.D. Deshpande and D.P. Giddens, "Turbulent Entrance Flow Using A Two-Equation Model," Physics of Fluids, Vol. 21, No. 3, pp. 510-512, March 1978.

2. A.M.A. Khalifa and D.P. Giddens; "Analysis of Disorder in Pulsatile Flows with Application to Poststenotic Blood Velocity Measurements in Dogs," Journal of Biomechanics , Vol. 11, No. 3, pp. 129-141, 1978.

3. R.A. Cassanova and D.P. Giddens; "Characterization of Flow Disorder Distal to Modeled Stenoses in Steady and Pulsatile Flow," Journal of Biomechanics, Vol. 11, pp. 441-453, 1978.

4. M.D. Deshpande and D.P. Giddens; "Turbulence Measurements in a Constricted Tube," Journal of Fluid Mechanics (in press).

5. J.I. Craig, V. Saxena, and D.P. Giddens; "A Minicomputer-Based Scheme for Turbulence Measurement with Pulsed Doppler Ultrasound," in Proceedings of the Third Annual Symposium on Computer Applications in Medical Care, Washington, D.C., October 1979 (in press).

6. Don P. Giddens; "Disorder in Pulsatile Flow: Biomedical Measurements with Hot Film, Laser and Ultrasound Anemometers," Proceedings of the Dynamic Flow Conference 1978, Dynamic Measurements in Unsteady Flows, pp. 705-735, published in Denmark (Box 121, DK-2740 Skovlunde), 1979.

7. A.M.A. Khalifa and D.P. Giddens; "Turbulence Measurements with Pulsed Doppler Ultrasound," in Proceedings of the First Mid-Atlantic Conference on Biofluid Dynamics, VPI and SU Press, Blacksburg, VA. 1978.

8. K. Balasubramanian, D.P. Giddens, and R.F. Mabon; "Steady Flow at the Carotid Bifurcation", Proceedings of the Second Mid-Atlantic Conference on Bio-fluid Mechanics, Plenum Press, ed. by D. Schneck (to be published in May, 1980).

C. Papers Under Review

1. A.M.A. Khalifa and D.P. Giddens; "Characterization and Evolution of Postenotic Flow Disturbances".

2. J.I. Craig, V. Saxena, and D.P. Giddens; "Ultrasonic Doppler Velocity Measurements by a Digital First Moment Demodulation Scheme - Application to Simulated Turbulence Signals".

D. Papers Presented

1. A.M.A. Khalifa and D.P. Giddens; "Turbulence Energy Spectra Measurement with Pulsed Doppler Ultrasound," First Mid-Atlantic Conference on Bio-Fluid Mechanics, Blacksburg, Va. August 1978.

2. "Disorder in Pulsatile Flow: Biomedical Measurements with Hot Film, Laser and Ultrasound Anemometers," Dynamic Flow Conference 1978, Johns Hopkins University, September, 1978. (invited)

3. A.M.A. Khalifa and D.P. Giddens; "Turbulence Energy Spectra Measurements with Pulsed Doppler Ultrasound," First International Conference on Mechanics in Medicine and Biology, Aachen, W. Germany, August 1978.

4. K. Balasubramanian, D.P. Giddens, and R. F. Mabon; "Steady Flow in a Model of the Human Carotid Bifurcation," 31st Annual Conference on Engineering in Medicine and Biology, Atlanta, Georgia, October 1978.

5. V. Saxena, J.I. Craig, and D.P. Giddens; "A Digital Method for Processing Doppler Ultrasound Signals," 31st Annual Conference on Engineering in Medicine and Biology, Atlanta, Georgia, October 1978.

6. "Hemodynamic Disorder and its Noninvasive Measurement," 31st Annual Conference on Engineering in Medicine and Biology, Atlanta, Georgia, October 1978. In Special Session on Cardiovascular Fluid Mechanics. (invited)

7. K. Balasubramanian, R.F. Mabon and D.P. Giddens; "Hemodynamics of the Carotid Artery," Annual AIChE Meeting, San Francisco, CA, November 1979.

8. A.M.A. Khalifa, R.F. Mabon, and D.P. Giddens; "Doppler Ultrasound Measurement of Two Turbulence Components," 32nd Annual Conference on Engineering in Medicine and Biology, Denver, CO., OCtober 1979.

9. A.M.A. Khalifa, R.F. Mabon, and D.P. Giddens; "Evolution of Disorder in Poststenotic Flows," 32nd Annual Conference on Engineering in Medicine and Biology, Denver, CO., October 1979.

10. "A Digital First Moment MEthod for Processing Doppler Ultrasound Signals," EUROMECH 118, Cardiovascular and Pulmonary Dynamics, Zuoz, Switzerland, 1979.

11. K. Balasubramanian, D.P. Giddens and R.F. Mabon; "Steady Flow at the Carotid Bifurcation", Second Mid-Atlantic Conference on Bio-Fluid Dynamics, VPI&SU, Blacksburg, VA., May 1980.